

**PATENT****IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Application No.: Not Assigned at Filing Date  
Filing Date: December 28, 2001  
Divisional of Application No.: 09/404,963  
Filed: September 24, 1999  
Applicant: Gregory M. Lanza, et al.  
Group Art Unit: 1619  
Examiner: M. Hartley  
Title: SITE SPECIFIC BINDING SYSTEM, IMAGING  
COMPOSITIONS AND METHODS  
Attorney Docket: 4375-000006/US/DVE

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Hon. Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

**PRELIMINARY AMENDMENT A**

This paper is filed as a preliminary amendment of the contemporaneously filed divisional application identified above. Please amend the claims in accordance with the following rewritten claims in clean form. Applicants include herewith an Attachment for claim amendments showing a marked up version of each amended claim in which underlines indicate insertions and brackets indicate deletions.

AMENDED CLAIMS REWRITTEN IN CLEAN FORM:

1. (Amended) A method for enhanced magnetic resonance imaging of a target tissue *in vivo* in a patient, the method comprising:

- (1) administering systemically to the patient,
  - (a) a site-specific ligand; and
  - (b) a liquid emulsion having an outer surfactant coating;

said ligand being conjugated to said liquid emulsion; wherein upon binding to the target tissue, the ligand-liquid emulsion conjugate enhances magnetic resonance imaging of the target tissue and

(2) detecting the enhanced magnetic resonance image of the ligand-liquid emulsion conjugate bound to the target tissue.

Please Cancel Claim 4 without prejudice or disclaimer.

8. (Amended) A composition for enhancing magnetic resonance imaging of a target tissue *in vivo* in a patient, said composition comprising:

- (a) a site-specific ligand; and
- (b) a liquid fluorocarbon emulsion having an outer surfactant coating;

said ligand being conjugated to said liquid emulsion wherein the composition is suitable for systemic administration to a patient and whereby upon imaging the target tissue by magnetic resonance, an enhanced image of the ligand-liquid emulsion conjugate bound to the target tissue can be detected.

Please add Claims 11-19.

11. (New) A method as set forth in claim 1 wherein said liquid emulsion is a perfluorocarbon emulsion.

12. (New) A method as set forth in claim 1 wherein said liquid emulsion additionally contains a chemotherapeutic agent.

13. (New) A method as set forth in claim 8 wherein said liquid emulsion is a perfluorocarbon emulsion.

14. (New) A method as set forth in claim 8 wherein said liquid emulsion additionally contains a chemotherapeutic agent.

15. (New) A composition for enhancing magnetic resonance imaging of a target tissue *in vivo* in a patient, said composition comprising:

(b) a site-specific ligand; and

(b) a liquid emulsion having an outer surfactant coating and a particle size between approximately 0.05 to 5 microns diameter;

said ligand being conjugated to said liquid emulsion wherein the composition is suitable for systemic administration to a patient and whereby upon imaging the target tissue by magnetic resonance, an enhanced image of the ligand-liquid emulsion conjugate bound to the target tissue is detected.

16. (New) A composition as set forth in claim 15 wherein said ligand is conjugated to said emulsion through an intervening chemical group.

17. (New) A composition as set forth in claim 16 wherein said intervening chemical group is constituted by a hydrocarbon spacer.

18. (New) A composition as set forth in claim 15 wherein said liquid emulsion is a perfluorocarbon emulsion.

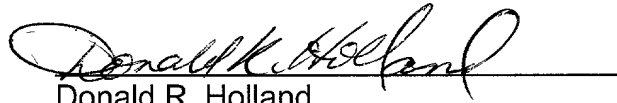
19. (New) A composition as set forth in claim 15 wherein said liquid emulsion additionally contains a chemotherapeutic agent.

**Remarks**

This paper amends claims 1 and 8, cancels claim 4 and adds new claims 11-19 so that claims 1-3 and 5-19 are pending in the case. No new matter is believed to be added by this amendment.

It is requested that the amendments to the claims be entered and that the case be examined on the merits. Should any questions arise, the P.T.O. is requested to contact the undersigned attorney.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Donald R. Holland", is written over a horizontal line.

Donald R. Holland  
Reg. No. 35,197  
Harness, Dickey & Pierce, P.L.C.  
7700 Bonhomme, Suite 400  
St. Louis, Missouri 63105  
(314) 726-7500

AMENDED CLAIMS IN MARKED UP VERSION:

1. (Amended) A method for [enhancing] enhanced magnetic resonance imaging of a target tissue [the acoustic reflectivity of a surface] *in vivo* in a patient, the method comprising:

(1) administering systemically to the patient [said surface]:

(a) a site-specific ligand; and

(b) a liquid emulsion having an outer surfactant coating [composed of a material selected from the group consisting of a natural or synthetic phospholipid, a fatty acid, cholesterol, lipolipid, sphingomyelin, tocopherol, glucolipid, stearylamine, cardiolipin, a lipid with ether or ether linked fatty acids and a polymerized lipid; said ligand being conjugated to said liquid emulsion] ; said ligand being conjugated to said liquid emulsion; wherein upon binding to the target tissue, the ligand-liquid emulsion conjugate enhances magnetic resonance imaging of the target tissue; and [whereby the resulting liquid emulsion conjugate is bound to said surface thereby causing enhancement of the acoustic reflectivity thereof for ultrasonic imaging or ultrasonic diagnostic applications]

(2) detecting an enhanced magnetic resonance image of the ligand-liquid emulsion conjugate bound to the target tissue.

8. (Amended) A composition for enhancing magnetic resonance imaging of a target tissue *in vivo* in a patient [formed *in vivo* and enhancing the acoustic reflectivity of a surface to which it is bound], said composition comprising:

(a) a site-specific ligand; and

(b) a liquid fluorocarbon emulsion having an outer surfactant coating [composed of a material selected from the group consisting of a natural or synthetic phospholipid, a fatty acid, cholesterol, lipolipid, sphingomyelin, tocopherol, glucolipid, stearylamine, cardiolipin, a lipid with ether or ether linked fatty acids and a polymerized lipid]; said ligand being conjugated to said liquid emulsion wherein the composition is suitable for systemic administration to a patient; and wherein upon imaging the target

tissue by magnetic resonance, an enhanced image of [with] the [resulting] ligand-liquid emulsion conjugate bound to the target tissue can be detected [being bound to said surface thereby causing enhancement of the acoustic reflectivity thereof for ultrasonic imaging or ultrasonic diagnostic applications].